Original Article

Effect of entropy-guided low-flow desflurane anaesthesia on laryngeal mask airway removal time in children undergoing elective ophthalmic surgery – A prospective, randomised, comparative study

Address for correspondence:
Dr. Renu Sinha,
All India Institute of Medical Sciences, RP Centre, Room No. 376, New Delhi - 110 029, India.
E-mail: renusinhaagarwal@gmail.com

Shivangi Mishra, Renu Sinha, Bikash Ranjan Ray, Ravinder Kumar Pandey, Vanlal Darlong, Jyotsna Punj

Department of Anaesthesiology, Pain Medicine and Critical Care, All India Institute of Medical Sciences, New Delhi, India

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_237_19

Quick response code

ABSTRACT

Background and Aims: In children, entropy-guided titration of isoflurane and sevoflurane leads to faster recovery after anaesthesia. However, role of entropy in recovery following desflurane anaesthesia is not known. Hence, we compared laryngeal mask airway (LMA) removal time and desflurane consumption with entropy and minimal alveolar concentration–guided titration in children given low-flow desflurane anaesthesia. **Methods:** After ethics committee approval and parental consent, 80 American Society of Anesthesiologists grade I–II children, age 2–14 years, undergoing elective ophthalmic surgery were randomised into entropy and minimal alveolar concentration–guided groups. After LMA insertion, anaesthesia was maintained using oxygen, air (FiO_2 0.5) and desflurane using low fresh gas flow of 0.75 L/min. In the entropy-guided group, desflurane was titrated to maintain state entropy between 40 and 60. In the minimal alveolar concentration–guided group, desflurane was titrated to maintain a minimal alveolar concentration between 1 and 1.3. We recorded LMA removal time (from switching off desflurane at the end of surgery till removal of LMA), haemodynamic parameters, uptake and consumption of desflurane between the groups. **Results:** LMA removal time was significantly decreased in the entropy-guided group in comparison to the minimal alveolar concentration–guided group (4.34 ± 2.03 vs 8.8 ± 2.33 min) ($P < 0.0001$). Consumption of desflurane was significantly less in the entropy-guided group compared with the minimal alveolar concentration–guided group (18.7 ± 5.07 vs 25.3 ± 8.11 mL) ($P < 0.0001$). **Conclusion:** Entropy-guided low-flow desflurane anaesthesia is associated with faster LMA removal and reduced consumption of desflurane in children undergoing ophthalmic surgery.

Key words: Children, consumption, desflurane, entropy, laryngeal mask airway, low-flow anaesthesia, minimum alveolar concentration

INTRODUCTION

Depth of anaesthesia is measured using monitors based on electroencephalography like bispectral index and entropy. Several studies have showed shorter recovery time and reduction in drug consumption in adults with anaesthesia depth monitoring compared with standard practice.[1-5] Desflurane is the least soluble of the inhaled anaesthetic agents, with a blood/gas partition coefficient of 0.42. Its pharmacokinetic properties and rapid metabolism make it effective for low-flow

How to cite this article: Mishra S, Sinha R, Ray BR, Pandey RK, Darlong V, Punj J. Effect of entropy-guided low-flow desflurane anaesthesia on laryngeal mask airway removal time in children undergoing elective ophthalmic surgery – A prospective, randomised, comparative study. Indian J Anaesth 2019;63:485-90.

systems. It offers advantage over other anaesthetic agents while using low-flow anaesthesia by causing minimal haemodynamic changes and reduced recovery time.[6-10] In children, limited studies have evaluated the effect of entropy-guided anaesthetic management using low-flow desflurane anaesthesia.

The present clinical study was designed as a prospective, randomised, comparative study with the primary outcome to compare laryngeal mask airway (LMA) removal time between entropy and minimum alveolar concentration (MAC)–guided maintenance of low-flow desflurane anaesthesia in children. Secondary outcomes were to compare desflurane consumption, cost analysis of desflurane consumed, haemodynamic and ventilator parameters, postoperative nausea vomiting, postoperative pain and emergence delirium in both the groups.

METHODS

The study was approved by the institutional ethics committee. This trial has been registered at Clinical Trial Registry of India (CTRI/2016/01/006567). Informed written consent and assent was taken from parents/legal guardian and/or child.

Children between 2 and 14 years of age, American Society of Anesthesiologists physical status I or II, undergoing elective ophthalmic surgery of 30–90 min duration using LMA were included in the study. Children on anticonvulsant, with mental retardation or premedicated with sedatives were excluded from the study. Children were evaluated a day before planned surgery in the ward. Children who fulfilled inclusion criteria were recruited in the study.

Standard fasting guidelines were advised to all children. Children were randomised using computer-generated random number tables into two groups, entropy-guided and MAC-guided, with 40 children in each group. In the entropy-guided group, low-flow desflurane anaesthesia was titrated by entropy values (GE Healthcare, Helsinki, Finland), and in the minimal alveolar concentration–guided group, titration was done by MAC values.

The children did not receive any premedication. In the operating room, standard monitors were applied. Anaesthesia was induced with fresh gas flow of 4 L/min of 100% O_2 with 8% sevoflurane through anaesthesia machine (Dräger Primus®; Drägerwerk AG & Co. KgaA, Lubeck, Germany). At loss of eyelash reflex, sevoflurane dial setting was reduced to 5%. Once adequate depth was achieved, entropy electrodes were applied on the forehead after cleaning and intravenous line was secured. Fentanyl 1 μg/kg and atracurium 0.25 mg/kg were administered intravenously, and appropriate size LMA was inserted and secured. The anaesthesiologist who further monitored and managed the child during the surgery was blinded to either MAC value (in entropy-guided group) or entropy value (in the MAC-guided group). For the entropy group, an opaque paper was applied on the desflurane marking on the vaporiser, MAC graph and reading on the monitor. For the MAC group, entropy reading was covered with an opaque paper. After the completion of the case, these readings were noted from the patient records in the monitor.

After confirmation of ventilation, sevoflurane was switched off and desflurane was started at 12% with fresh gas flow of 4 L/min (1.5 L/min O_2 and 2.5 L/min air with FiO_2 of 0.5), and controlled ventilation was initiated to maintain end-tidal carbon dioxide between 30 and 40 mmHg. Once 'equilibration point' [ratio of expired/inspired desflurane (FeD/FiD) of 0.8] was achieved, fresh gas flow was reduced to 0.75 L/min (0.47 L/min O_2 and 0.28 L/min air, FiO_2 of 0.5). Perioperative analgesia and relaxation were managed with intravenous fentanyl, paracetamol 15 mg/kg and atracurium, respectively. Ondansetron 100 μg/kg was administered for postoperative nausea and vomiting prophylaxis.

In the entropy-guided group, dial setting of the desflurane vaporiser was adjusted to maintain state entropy between 40 and 60. In the MAC-guided group, adjustment of the dial setting was titrated to maintain target MAC value between 1 and 1.3. Any change in heart rate (HR) or blood pressure (BP) >20% outside the target range of entropy or MAC or difference between response entropy and state entropy of more than 10 was managed with 0.5 μg/kg fentanyl. At the end of surgery, vaporiser was switched off and fresh gas flow was increased to 6 L/min. At the start of respiratory effort, reversal agent (neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg) was administered. LMA was removed at awakening (facial grimace, spontaneous eye opening and/or purposeful arm movement). LMA removal time was defined as the time from switching off the desflurane till the time for LMA removal. The child was shifted to the postanaesthesia care unit. The amount of desflurane, sevoflurane, O_2 and air uptake and consumption was noted from the anaesthesia machine.

Haemodynamic parameters, that is, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were monitored continuously and noted at every 5 min interval including baseline, at intravenous cannula insertion and at LMA insertion. Ventilatory parameters, that is, end-tidal carbon dioxide and oxygen saturation, were recorded at every 5 min interval; also, baseline level, expired/inspired desflurane, MAC values and entropy value (state and response) were recorded every 5 min till the removal of LMA. Paediatric Anaesthesia Emergence Delirium score (PAEDS) was noted at awakening and every 5 min till discharge from the postanaesthesia care unit.[11] If PAEDS was 10 or more, then midazolam bolus of 0.4 mg/kg was administered, not exceeding 10 mg. Modified Aldrete score was recorded every 5 min till modified Aldrete score of more than 9 was achieved and the child was discharged from the postanaesthesia care unit.[12] Modified CHEOPS score was recorded every 5 min in the postoperative period till discharge from the postanaesthesia care unit.[13] Any complain of nausea and/or vomiting in the postoperative period was recorded and postoperative nausea and vomiting scoring was done. Metoclopramide 100 μg/kg was administered if postoperative nausea and vomiting score ≥2.[14]

According to the results of a previous study[15] to detect a reduction of 20% in LMA removal time with α of 0.05 and statistical power of 0.9, assuming a minimum difference of 2 min in LMA removal time to be clinically significant, at least 33 children needed to be enrolled in each group. For more reliability and clinical reproducibility, we included 40 children in each group.

Statistical analysis

Data were analysed using statistical software STATA 14.0. Quantitative data that followed normal distribution were expressed as mean ± standard deviation. Quantitative data that followed skewed distribution were expressed as median (minimum and maximum). Qualitative categorical data were represented as frequency and percentage. Independent *t*-test and Mann–Whitney *U*-test were used to compare the quantitative variable that followed normal and skewed distribution, respectively. Chi-square test/Fisher's exact test was used to test the proportion between groups. General estimation equation was used to compare change over period of time. $P < 0.05$ was considered as statistical significance.

RESULTS

We screened 120 patients for inclusion in the study, of which 80 patients were included in the study and were randomly allocated into two groups [Figure 1]. The groups were comparable with reference to age, weight, sex, indication of surgery and duration of procedure [Table 1].

LMA removal time was significantly less in the entropy-guided group (4.34 ± 2.03 min) when compared with the MAC-guided group (8.8 ± 2.33 min) with a difference of 4.46 min and 95% confidence interval (3.49, 5.43) [Table 2].

Consumption and uptake of desflurane and oxygen was significantly less in the entropy-guided group compared with the MAC-guided group [Table 3]. Entropy values were significantly lower in the MAC-guided group [Figure 2], whereas MAC values and end-tidal desflurane were found to be significantly lower in the entropy-guided group [Figure 3]. In the MAC-guided group, MAC of 1–1.3 corresponded to response entropy values between 30 and 40 and state entropy values between 20 and 30. In the entropy-guided group, entropy values between 40 and 60 corresponded to MAC between 0.6 and 0.8 throughout the surgery.

There was no significant difference in HR and arterial oxygen saturation in both the groups. SBP, DBP and

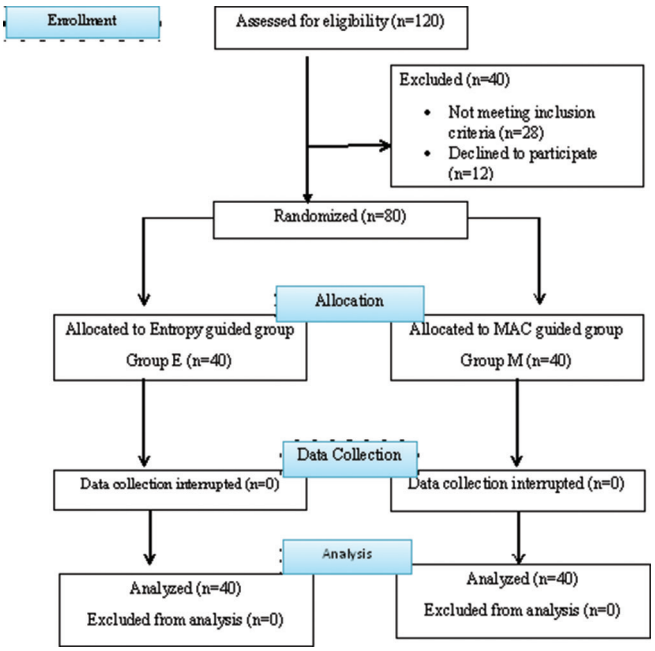

Figure 1: Consort diagram

Table 1: Demographic data

Variable	Minimum alveolar concentration-guided group, *n*=40 (%)	Entropy-guided group, *n*=40 (%)
Age, years		
Mean±SD (median)	7.9±2.88 (8)	8.65±3.25 (8)
(95% CI)	(6.98, 8.82)	(7.61, 9.69)
Weight, kg		
Mean±SD (median)	22.02±8.88 (20)	23.9±9.25 (23.5)
(95% CI)	(19.18, 24.86)	(20.94, 26.86)
Sex		
Male	25 (62.5)	32 (80.0)
Female	15 (37.5)	8 (20.0)
Indication of surgery		
Cataract	18 (45.0)	20 (50.0)
Squint	17 (42.5)	13 (32.5)
Glaucoma	1 (2.5)	2 (5.0)
Cornea	4 (10.0)	2 (5.0)
Oculoplasty	0 (0.0)	3 (7.5)
Duration of procedure, minutes	56.6±14.1 (53) (52.09, 61.11)	55.8±15.4 (53) (50.87, 60.72)
Mean±SD (median) (95% CI)		

SD – Standard deviation; CI – Confidence interval

Table 2: LMA removal time

Groups	LMA removal time (min)				*P* (95%* CI)
	Minimum	Maximum	Mean±SD (95% CI)	Median	
Minimum alveolar concentration-guided group, *n*=40	5.1	14.1	8.80±2.33 (8.05, 9.54)	9.15	<0.0001 (3.49, 5.43)
Entropy-guided group, *n*=40	1.9	12.7	4.34±2.03 (3.69, 4.99)	3.75	

LMA – Laryngeal mask airway; SD – Standard deviation; CI – Confidence interval, **P*<0.05 statistically significant

Table 3: Uptake and consumption of anaesthetic agents and gases

Variable	Minimum alveolar concentration-guided group, *n*=40, mean±SD (95% CI)	Entropy-guided group, *n*=40, mean±SD (95% CI)	*P* (95% CI)
Uptake of desflurane, mL	5.9±2.25 (5.18, 6.62)	4.6±2.28 (3.87, 5.32)	0.019 (0.24, 2.26)
Uptake of sevoflurane, mL	2.2±0.99 (1.88, 2.52)	2.1±1.12 (1.74, 2.46)	0.444 (−0.34, 0.59)
Consumption of desflurane, mL	25.3±8.11 (22.71, 27.89)	18.7±5.07 (17.08, 20.32)	<0.0001 (3.51, 9.53)
Consumption of sevoflurane, mL	10.4±4.33 (9.02, 11.78)	9.9±4.89 (8.34, 11.46)	0.296 (−1.56, 2.56)
Consumption of oxygen, mL	105.3±18.84 (99.27, 111.32)	82.3±17.53 (76.69, 87.91)	<0.0001 (14.86, 31.09)
Consumption of air, mL	27.4±9.78 (24.27, 30.53)	27.2±8.61 (24.47, 29.95)	0.934 (−3.85, 4.35)

SD – Standard deviation; CI – Confidence interval. *P*<0.05 statistically significant

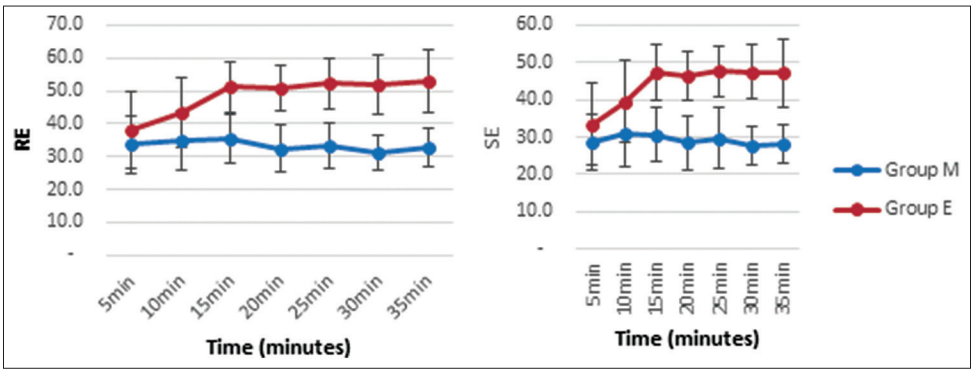

Figure 2: Intraoperative response and state entropy values in MAC-guided (M) and entropy-guided (E) groups

MAP were significantly lower in the MAC-guided group compared with the entropy-guided group. Three patients in the entropy-guided group and four patients in the MAC-guided group required fentanyl bolus once intraoperatively which was not statistically significant.

No difference was seen in other haemodynamic and ventilator parameters in intraoperative or postoperative period. No difference was seen in the incidence of postoperative nausea and vomiting, emergence delirium, modified Aldrete score, postoperative pain and any other interventions (i.e., fentanyl, midazolam, ondansetron) in both the groups [Table 4].

DISCUSSION

The primary outcome of our study was to compare LMA removal time between entropy and MAC-guided maintenance of low-flow desflurane anaesthesia in children. We obtained a 50% reduction in LMA removal time with a difference of 4.46 min [95% confidence interval (3.49, 5.43)] when desflurane was titrated using entropy values compared with MAC values. Although 4.46 min may not be clinically significant for a single case, in a high-volume centre like ours with at least 20 cases carried out per day, this difference when extrapolated to the number of cases done in a day in operating room will result in clinically relevant difference.

Choi SR *et al*.[15] compared time to spontaneous eye opening following switching off sevoflurane by standard and entropy value in children between 3 and 12 years undergoing tonsillectomy or adenoidectomy surgery. They used midazolam premedication and O_2, air and sevoflurane at fresh gas flow of 1.5 L/min. They found that spontaneous eye opening was faster with entropy group with a difference of 3.7 min. Use of midazolam premedication, sevoflurane and low target entropy values of 40–50 might be the cause of smaller difference in time to spontaneous eye opening when compared with our study.

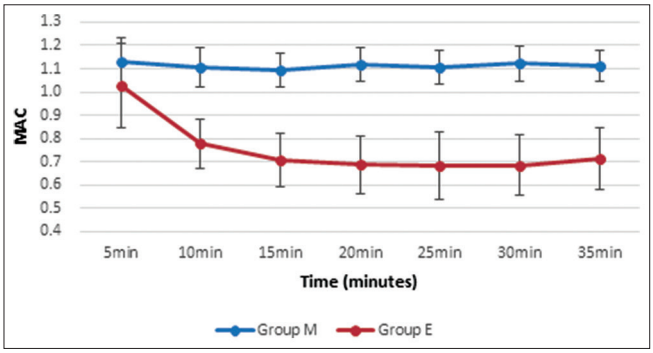

Figure 3: Intraoperative minimum alveolar concentration in MAC-guided (M) and entropy-guided (E) groups

Table 4: Postoperative intervention

Intervention	Group M, *n*=40 (%)	Group E, *n*=40 (%)	*P*
Fentanyl	3 (7.5)	2 (5.0)	0.99
Midazolam	8 (20.0)	4 (10.0)	
Metochlopramide	1 (2.5)	0 (0)	

*P<0.05 statistically significant

Talawar P *et al*.[16] found a difference of 2.72 min in time to awakening following switching off isoflurane in a study on 50 children of 2–12 years age undergoing lower abdomen urologic surgeries comparing entropy values to standard method (HR and MAP) for titration of isoflurane (with O_2 0.5 L/min and N_2O 0.5 L/min). Shorter difference in time to awakening in this study may be due to use of isoflurane and possible bias due to use of standard methods to titrate depth of anaesthesia as vital parameters can change due to pain, awareness and lighter plane of anaesthesia. We used entropy and MAC value to avoid bias by the attending anaesthesiologist. Desflurane has lower blood gas solubility in comparison to isoflurane, which may have contributed to faster recovery in our study.

We also found a 24% reduction in consumption of desflurane when anaesthesia was titrated using entropy compared with MAC values with a difference of 7 mL. This observation was comparable to studies done previously in adults and children.[2-4,17] With desflurane costing INR 35.8/mL in India, a difference of 7 mL/case amounts to saving of INR 250 per case. This when extrapolated to whole day with a minimum of 20 cases done at our centre will lead to saving of minimum INR 5000 per day. In long term, this cost reduction will be economical for a developing country like India.

In our study, there was a comparatively higher consumption of O_2 in the MAC-guided group compared with the entropy-guided group. This was due to significantly longer LMA removal time in the MAC-guided group when 100% O_2 was used at a flow of 6 L/min.

In our study, no significant difference was seen in HR; however, SBP, DBP and MAP were found to be significantly lower in the MAC-guided group in comparison to the entropy-guided group during surgery. This may be due to higher MAC resulting in higher consumption of desflurane in the MAC-guided group.Variable haemodynamic parameters have been found in studies comparing entropy or bispectral index with standard practice group (clinical parameters such as HR, BP). This might be due to various confounding factors in different studies such as use of N_2O,[3] use

of tourniquet[4] and different modes of analgesia, that is, continuous infusion[18] or intermittent bolus of opioids[3,19] or regional anaesthesia.[19]

There was no significant difference in CHEOPS score, modified Aldrete score at any point of time postoperatively. Although postoperative nausea and vomiting score was higher in the MAC-guided group, the difference was not statistically significant. Higher postoperative nausea and vomiting scores in the MAC-guided group might be due to higher number of squint surgery in comparison to the entropy-guided group.

The limitation of our study was most of the cases were less than 1 h mean duration of surgery in both groups. Thus, the results of our study cannot be generalised to longer duration surgeries.

CONCLUSION

We conclude that in children undergoing ophthalmic surgery of less than 1 h, entropy-guided titration of anaesthesia using low-flow desflurane, air and O_2 anaesthesia resulted in faster LMA removal, reduced consumption of desflurane and lesser haemodynamic variation in comparison to MAC-guided titration of anaesthesia.

Acknowledgement

The authors thank Dr. Chandralekha, ex-HOD of Anaesthesiology and Critical Care, and Dr. Rohit Saxena, professor of ophthalmology, for their support and guidance.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sargin M, Uluer MS, Ozmen S. The effects of bispectral index monitoring on hemodynamics and recovery profile in developmentally delayed pediatric patients undergoing dental surgery. PaediatrAnaesth 2015;25:950-5.
2. Song D, Joshi GP, White PF. Titration of volatile anesthetics using bispectral index facilitates recovery after ambulatory anesthesia. Anesthesiology 1997;87:842-8.
3. Aimé I, Verroust N, Masson-Lefoll C, Taylor G, Laloë PA, Liu N, *et al*. Does monitoring bispectral index or spectral entropy reduce sevoflurane use? Anesth Analg 2006;103:1469-77.
4. Wu SC, Wang PC, Liao WT, Shih TH, Chang KA, Lin KC, *et al*. Use of spectral entropy monitoring in reducing the quantity of sevoflurane as sole inhalational anesthetic and in decreasing the need for antihypertensive drugs in total knee replacement surgery. Acta AnaesthesiolTaiwanica 2008;46:106-11.
5. Hor TE, Linden PVD, Hert SD, Mélot C, Bidgoli J. Impact of entropy monitoring on volatile anesthetic uptake. J Am Soc Anesthesiol 2013;118:868-73.
6. Baum JA, Aitkenhead AR. Low-flow anaesthesia. Anaesthesia 1995;50:37-44.
7. Baum J, Berghoff M, Stanke HG, Petermeyer M, Kalff G. Low-flow anesthesia with desflurane. Anaesthesist 1997;46:287-93.
8. JeongJS, Yoon SW, Choi SL, Choi SH, Lee BY, Jeong MA. Comparison of emergence times with different fresh gas flow rates following desflurane anaesthesia. JInt Med Res 2014;42:1285-93.
9. Xie G, Jiang H. Clinical study of desflurane on low flow anesthesia compared with sevoflurane and enflurane. Chin Med J (Engl) 1997;110:707-10.
10. Nel MR, Ooi R, Lee DJ, Soni N. New agents, the circle system and short procedures. Anaesthesia 1997;52:364-7.
11. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 2004;100:1138-45.
12. Aldrete JA. Modifications to the postanesthesia score for use in ambulatory surgery.J PerianesthesiaNurs 1998;13:148-55.
13. McGrath PJ Johnson G. CHEOPS: A behavioral scale for rating postoperative pain in children.Adv Pain ResTher 1985;9:395-402.
14. Subramaniam B, Madan R, Sadhasivam S, Sennaraj B, Tamilselvan P, Rajeshwari S, *et al*. Dexamethasone is a cost-effective alternative to ondansetron in preventing PONV after paediatric strabismus repair. Br J Anaesth 2001;86:84-9.
15. Choi SR, Lim YH, Lee SC, Lee JH, Chung CJ. Spectral entropy monitoring allowed lower sevoflurane concentration and faster recovery in children. Acta AnaesthesiolScand 2010;54:859-62.
16. Talawar P, Chhabra A, Trikha A, Arora MK, Chandralekha. Entropy monitoring decreases isoflurane concentration and recovery time in pediatric day care surgery -a randomized controlled trial. Pediatr Anesth 2010;20:1105-10.
17. Ibrahim TH, Yousef GT, Hasan AMA, Eldesuky HI. Effect of bispectral index monitoring on desflurane consumption and recovery time in morbidly obese patients undergoing laparoscopic sleeve gastrectomy. Anesth Essays Res 2013;7:89-93.
18. Bruhn J, Kreuer S, Bischoff P, Kessler P, Schmidt GN, Grzesiak A, *et al*. Bispectral index and A-line AAI index as guidance for desflurane-remifentanil anaesthesia compared with a standard practice group: A multicentre study. Br J Anaesth 2005;94:63-9.
19. Bannister CF, BrosiusKK, Sigl JC, Meyer BJ, Sebel PS. The effect of bispectral index monitoring on anesthetic use and recovery in children anesthetized with sevoflurane in nitrous oxide. Anesth Analg 2001;92:877-81.